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Title: Computational engineering of Human Apolipoprotein for enhanced interaction with bacterial toxins

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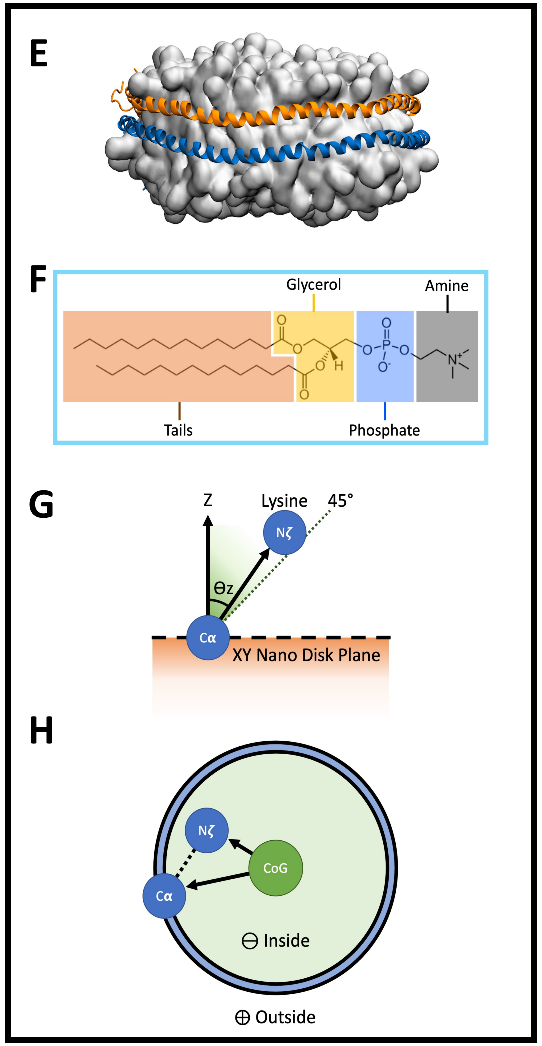
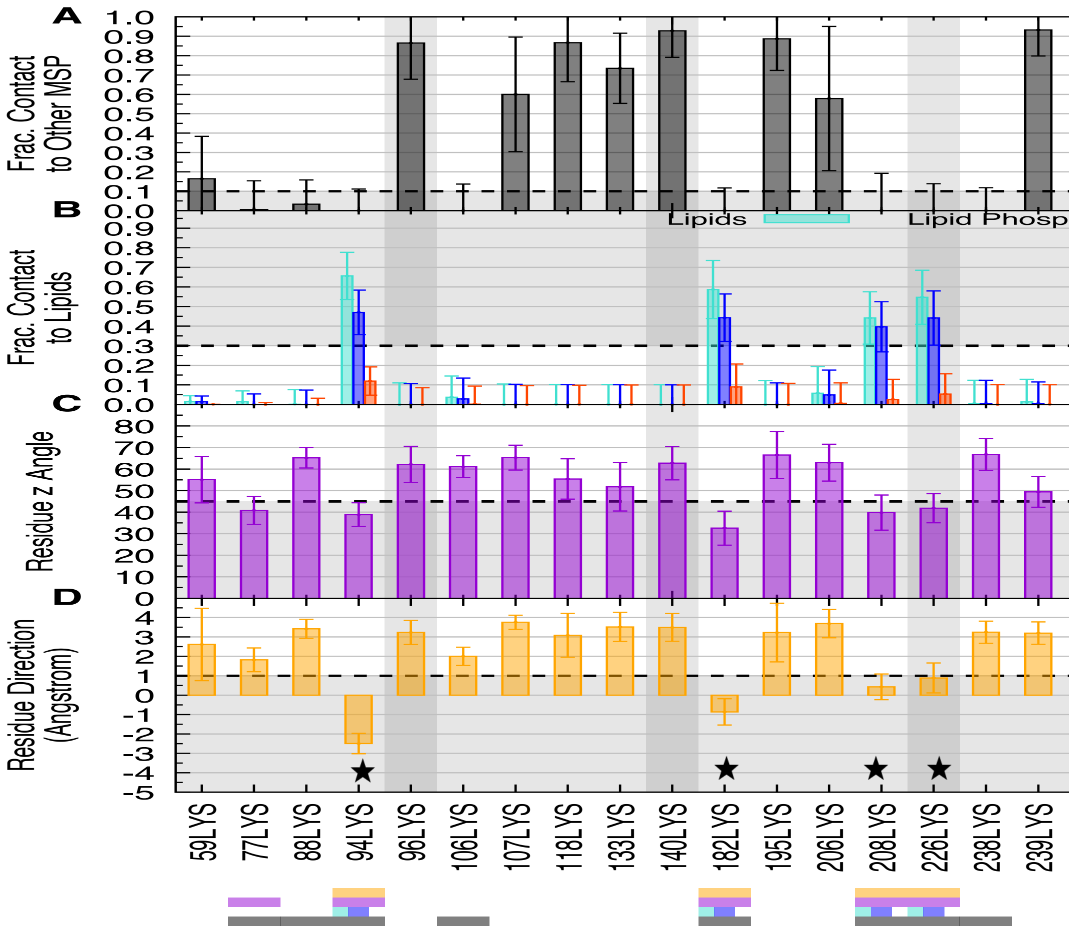
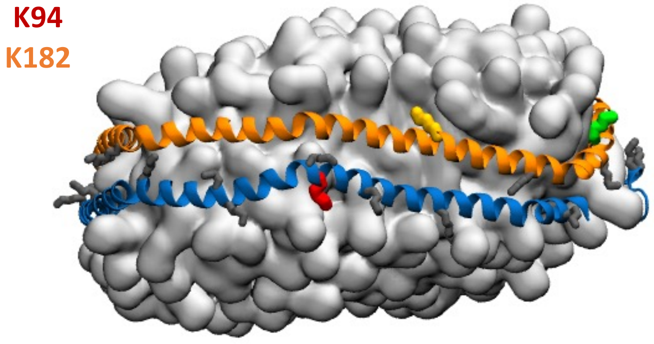
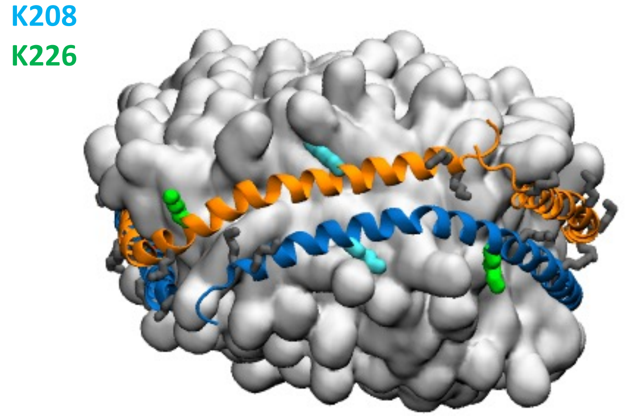




Of the 17 lysine residues on the 1D1 MSP individual protein chains, there are 4 promising candidates for mutation that meet our criteria.





Abstract

Sepsis is caused by an over-activation of the immune system in response to the presence of bacterial endotoxins in the bloodstream. LPS exemplifies a potent immune stimulator which can lead to an excessive activation leading to an overly pro-inflammatory reaction and if left untreated results in multi-organ failure and death. Human lipoproteins (HLP) have been shown to neutralize LPS and facilitate its clearance from circulation via the liver. However, host-derived lipoproteins are inhomogeneous in content and size, presenting a challenge for therapeutic applications.

In this work, we have used IC facilities in order to computationally engineer HLP for an enhanced interaction with LPS. This work is a continuation of our previous efforts to derive an optimal Nanodisc (ND) lipid mixture for enhanced association with the endotoxin. We have performed fully atomistic Molecular dynamic (MD) simulations in order to carefully identify the most optimal residues in HLP, which can potentially lead to a stronger association to LPS.